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Exhibit A

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: AOKI et al) Examiner: Anish Gupta
Serial Number: 09/490,756) Art Unit: 1653
Filed: January 24, 2000)
For: METHOD FOR TREATING DYSTONIA)
WITH BOTULINUM TOXIN TYPE B) Irvine, California

DECLARATION UNDER 37 C.F.R. SECTION 1.132

I, MITCHELL F. BRIN, declare as follows:

1. I am over the age of twenty one, competent to testify in a court of law, and could and would testify to the matters set forth below before the United States Patent and Trademark Office, if required to do so.

2. I understand that this declaration will be used to assist prosecution of United States patent application serial number 09/490,756, including to assist to overcome a rejection in the November 8, 2000 office action in serial number 09/490,756 based upon a mode or capability of operation attributed to a reference.

3. I graduated from the University of Pennsylvania in 1975 with a bachelor of arts in biology (Magna Cum Laude and Phi Beta Kappa) and I received an M.D. degree from the Columbia College of Physicians and Surgeons. I completed neurology and fellowship training at the Columbia University Neurological Institute. In 1994, I joined the Mount Sinai Medical Center as an Associate Professor and Director of the Movement Disorders Program.

I was most recently, attending Physician and Associate Professor of Neurology at the Mount Sinai School of Medicine in New York where I also served as Director of Movement Disorders and held the Bachmann-Strauss Endowed Chair in Neurology. I have directed numerous neurological research programs relating to use of a botulinum toxin in the treatment of movement disorders, such as dystonia.

I was one of the first investigators to examine the use of botulinum toxin for the treatment of medical disorders and I pioneered the use of botulinum toxin for the

treatment of dystonias, including blepharospasm and other debilitating neurological disorders. I have designed and conducted double blind studies examining the use of botulinum toxin for numerous conditions, and have conducted a number of multicenter studies for uses of botulinum toxin.

I founded the American Academy of Neurology course on botulinum toxin, and I have organized numerous courses and symposia on botulinum toxin, and has published extensively on this subject.

I hold many appointments and affiliations, including President and Founder of WE MOVE, an international professional and patient educational not-for-profit organization that focuses on movement disorders. I also serve on the board of directors of the Bachmann-Strauss Dystonia and Parkinson Foundations and the Exceptional Parent Foundation. I serve on the review board of the United States Pharmacopeial Convention and the Steering Committee of the World Congress on Disabilities. I am a member of the American Academy of Neurology Section on Movement Disorders and Co-Founder of the Dystonia Study Group.

I also serve on the editorial and peer-review boards of numerous scientific journals and on the steering committee of the World Congress on Disabilities. I am the recipient of many awards including being elected a Fellow to the American Academy of Neurology; recipient of the FDA's Commissioner's Special Citation for my work with neurological movement disorders; and a Distinguished Service and Honor Award from the American Otolaryngology Society.

A partial list of my publications is attached to this declaration as Appendix A.

By training and experience I am an expert in the therapeutic use of the botulinum toxins, including use of botulinum toxin type B to treat dystonia.

4. I am currently employed by Allergan, Inc, the assignee of the above-identified patent application, as Vice President, *Botox*[®]/Neurology. In this capacity, I oversee the *Botox*[®] (botulinum toxin type A purified neurotoxin complex) development portfolio, and direct clinical programs for uses of the botulinum toxins.

5. I am the co-author of Jankovic J, and Brin M., *Therapeutic Uses of Botulinum Toxin*, New Eng J. Med, 1186-1194;1991 (the "Jankovic reference").

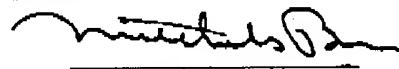
6. The Jankovic reference discusses therapeutic uses of *only* type A botulinum toxin. As of the April 25, 1991 date of the Jankovic reference it was completely unknown as to whether or not botulinum toxin type B would have any therapeutic efficacy in human. Indeed, as far as I am aware, the first reported use of type B botulinum toxin in humans did not occur until 1995.

7. Additionally, the Jankovic reference does not state that botulinum type B can be used as an alternative or in place of botulinum type A, although it does speculate on page 1189, that other botulinum toxins, immunologically distinct from the type A toxin, may have some utility to treat patients who have become non-responsive to type A toxin due to a development of antibodies to the type A toxin.

8. In my opinion, prior to December 28, 1993, it would have been foolhardy and dangerous to use botulinum toxin type B to treat patients with dystonia, such as cervical dystonia, in light of the complete lack of clinical experience with the type B toxin as of that date. Certainly, the 1991 Jankovic reference does not teach, suggest, motivate or recommend use of botulinum toxin type B by physicians to treat any dystonic patients.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that any such willful false statements may jeopardize the validity of the above-identified application or any patent issuing therefrom.

Executed this 8 day of February 2001, at Irvine, California.



Mitchell F. Brin

ATTACHMENT A**PUBLICATIONS OF MITCHELL F BRIN****A. Original, Peer Reviewed Publications**

1. Wormser GP, Donath J, Kennish A, Brin MF, Sanders M. Fatal pneumonia. *NYS J Med* 1981;1088-1089.
2. †Brin MF, Fetell MR, Green PHA, Kayden HJ, Hays AP, Behrens MM, Baker H. Blind loop syndrome, vitamin E malabsorption, and spinocerebellar degeneration. *Neurology* 1985;35:338-342.
3. Bressman S, Fahn S, Eisenberg M, Brin M, Maltese W. Biotin-responsive encephalopathy with myoclonus, ataxia, and seizures. *Adv Neurology* 1985;43:119-125
4. Lange DJ, Warner C, Brin M, List T, Fahn S, Lovelace RE. Botulinum toxin therapy: distant effects on neuromuscular transmission. *Muscle Nerve* 1985;8:624-625.
5. Blitzer A, Lovelace RE, Brin MF, Fahn S, Fink ME. Electromyographic findings in focal laryngeal dystonia (spastic dysphonia). *Ann Oto, Rhino, and Laryngoscope* 1985; 94:591-594.
6. † Brin MF, Pedley TA, Lovelace RE, Emerson RG, Gouras P, MacKay C, Kayden HJ, Levy J, Baker H. Electrophysiological features of abetalipoproteinemia: functional consequences of vitamin E deficiency. *Neurology* 1986; 36:669-673.
7. Breakefield XO, Bressman SB, Kramer PL, Ozelius LO, Moskowitz C, Tanzi R, Brin MF, Hobbs W, Kaufman D, Kidd KK, Fahn S, Gusella J. Linkage analysis in a family with dominantly inherited torsion dystonia: Exclusion of the pro-opiomelanocortin and glutamic acid decarboxylase genes, and other chromosomal regions using DNA polymorphisms. *J Neurogenetics* 1986;3:159-175.
8. Burke RE, Brin MF, Fahn S, Bressman SB, Moskowitz C. An analysis of the clinical course of non-Jewish autosomal dominant torsion dystonia. *Movement Disorders* 1986;1:163-178.
9. Blitzer A, Brin MF, Fahn S, Lange D, Lovelace RE. Botulinum toxin for the treatment of spastic dysphonia. *Laryngoscope* 1986;96:1300-1301.
10. Lange DJ, Brin M, Warner C, Fahn S, Lovelace RE. Distant effects of local

injections of botulinum toxin. *Muscle Nerve* 1987;10:552-555.

11. † Brin MF, Fahn S, Moskowitz CB, Blitzer A, Friedman A, Shale HM, Greene PE, List T, Lange D, Lovelace RE, McMahon D. Localized injections of botulinum toxin for the treatment of focal dystonia and hemifacial spasm. *Movement Disorders* 1987;2:237-254.
12. de Yebenes JG, Brin MF, Mena MA, De Felipe C, del Rio MR, Bazan E, Martinez A, Fahn S, del Rio J, Vazquez A. Neurochemical findings in neuroacanthocytosis. *Movement Disorders* 1988;3:300-312.
13. Blitzer AB, Brin MF, Fahn S, Lovelace RE. Localized injections of botulinum toxin for the treatment of focal laryngeal dystonia (spastic dysphonia). *Laryngoscope* 1988;98:193-197.
14. Blitzer AB, Brin MF, Fahn S, Lovelace RE. Clinical and laboratory characteristics of laryngeal dystonia: A study of 110 cases. *Laryngoscope* 1988;98:636-640.
15. Vatassery GT, Brin MF, Fahn S, Kayden HJ, Traber MG. Effect of high doses of dietary vitamin E on concentrations of vitamin E in several brain regions, plasma, liver and adipose tissue. *J Neurochem* 1988;51:621-623.
16. Kaplan JG, Pack MD, Horoupian D, DeSouza T, Brin MF, Schaumburg H. Distal axonopathy associated with chronic gluten enteropathy: A treatable disorder. *Neurology* 1988;38:642-645.
17. Younger DS, Chou S, Hays AP, Lange DJ, Emerson R, Brin MF, Thompson H, Rowland, LP. Primary lateral sclerosis: A clinical diagnosis re-emerges. *Arch Neurol* 1988;45:1304-7.
18. Blitzer A, Brin MF, Fahn S. Botulinum toxin injection for the treatment of oromandibular dystonia. *Ann Oto Rhino Laryngol* 1989;98:93-97.
19. † Brin MF, Blitzer A, Fahn S, Gould W, Lovelace RE. Adductor laryngeal dystonia (spastic dysphonia): Treatment with local injections of botulinum toxin (BOTOX). *Movement Disorders* 1989;4:287-296.
20. Ozelius L, Kramer PL, Moskowitz CB, Kwaitkowski J, Brin MF, Bressman SB, Schuback DE, Falk CT, Risch N, de Leon D, Burke RE, Haines J, Gusella JF, Fahn S, Breakefield XO. Human gene for torsion dystonia located on chromosome 9q32-q34. *Neuron* 1989;2:1427-1434.
21. Bressman SB, de Leon D, Brin MF, Risch N, Burke RE, Greene PE, Shale H, Fahn S. Idiopathic dystonia among Ashkenazi Jews: Evidence for autosomal dominant inheritance. *Ann Neurol* 1989;26:612-620.
22. † Brin MF, Fahn S, Loftus S, McMahon D, Flaster E. Relationship between dose of vitamin E administered and blood level. *Ann NY Acad Sci* 1989;570:421-424.

23. Parkinson Study Group. DATATOP: A multi-center controlled clinical trial in early Parkinson's disease, *Archives of Neurology* 1989; 46:1052-1060.
24. Parkinson Study Group. Effect of deprenyl on the progression of disability in early Parkinson's disease. *New England Journal of Medicine* 1989; 321:1364-1371.
25. Kramer PL, de Leon D, Ozelius L, Risch N, Brin MF, Bressman SB, Burke RE, Kwiatkowski DJ, Schuback DE, Shale H, Gusella JF, Breakefield XO, Fahn S. Dystonia gene in Ashkenzi Jewish population located on chromosome 9q32-34. *Ann Neurol* 1990;27:114-120.
26. Greene P, Kang U, Fahn S, Brin MF, Moskowitz C, Flaster. Double-blind, placebo controlled trial of botulinum toxin injection for the treatment of spasmodic torticollis. *Neurology* 1990;40:1213-1218.
27. Risch NJ, Bressman SB, de Leon D, Brin MF, Burke RE, Greene PE, Shale H, Claus E, Cupples LA, Fahn S. Segregation analysis of idiopathic torsion dystonia in Ashkenazi Jews suggests autosomal dominant inheritance. *Am J Hum Genet* 1990;46:533-538.
28. † American Academy of Neurology. Assessment: The clinical usefulness of botulinum toxin-A in treating neurological disorders; Report of the Therapeutics and Technology Assessment Subcommittee Committee of the American Academy of Neurology. (MF Brin, Facilitator of report) *Neurology*, 1990;40:1332-1336.
29. American Academy of Otolaryngology-Head and Neck Surgery. Academy policy statement: Botox for spasmodic dysphonia. *AAO-HNS Bulletin* 1990;9:8.
30. Jankovic J, McDermott M, Carter J, Gauthier S, Goetz C, Golbe L, Huber S, Koller W, Olanow C, Shoulson I, Stern M, Tanner C, Weiner W and the Parkinson Study Group. Variable expression of Parkinson's disease: a base-line analysis of the DATATOP cohort. *Neurology* 1990; 40:1529-1534.
31. Saint-Hilaire MH, Burke RE, Bressman SB, Brin MF, Fahn S. Delayed onset dystonia due to perinatal or early childhood asphyxia. *Neurology*, 1991;41:216-222.
32. Blitzler A, Brin MF. Laryngeal dystonia: a series with botulinum toxin therapy. *Ann Oto Rhino Laryngol* 1991; 100:85-89.
33. Lange DJ, Rubin M, Greene PE, Kang UJ, Moskowitz CB, Brin MF, Lovelace RE, Fahn S. Distant effects of locally injected botulinum toxin: A double-blind study of single fiber EMG changes. *Muscle Nerve* 1991;14:672-675.

34. Jankovic J, Brin MF. Therapeutic applications of botulinum toxin. *NEJM* 1991;324:1186-1194.
35. Kwaitkowski DJ, Nygaard TG, Schuback DE, Perman S, Trugman JM, Bressman SB, Burke RE, Brin MF, Ozelius L, Breakefield XO, Fahn S and Kramer PL. Identification of a highly polymorphic microsatellite VNTR within the argininosuccinate synthetase locus: exclusion of the dystonia gene on 9q32-34 as the cause of dopa-responsive dystonia in a large kindred. *Am J Hum Genet* 1991;48:121-128.
36. Chan J, Brin MF, Fahn S. Idiopathic cervical dystonia: clinical characteristics. *Movement Disorders* 1991;6:119-126.
37. Glickman RM, Glickman JN, Magun A, Brin M. Apolipoprotein synthesis in normal and abetalipoproteinemic intestinal mucosa. *Gastroenterology* 1991;101:749-755.
38. Schuback D, Kramer P, Ozelius L, Holmgren G, Forsgren L, Kyllerman M, Wahlstrom J, Craft CM, Nygaard T, Brin MF, de Leon D Bressman S, Moskowitz CB, Burke RE, Sanner G, Drugge U, Gusella J, Fahn S and Breakefield XO. Dopamine beta-hydroxylase gene excluded in four subtypes of hereditary dystonia. *Hum Genet* 1991;87:311-316.
39. Ozelius L, Kramer P, de Leon D, Risch N, Bressman S, Schuback D, Brin MF, Kwaitkowski D, Burke R, Gusella JF, Fahn S, Breakefield XO. Strong allele association between ASS allele and torsion dystonia gene (DYT1) and loci on chromosome 9q34 in Ashkenazi Jews. *Am J Hum Genet* 1992;50:619-628.
40. Blitzer A, Brin MF, Stewart C, Aviv JE, Fahn S. Abductor laryngeal dystonia: a series treated with botulinum toxin. *Laryngoscope* 1992;102: 163-167.
41. LeWitt PA, Galloway MP, Matson W, Milbury P, McDermott M, Srivastava DK, Oakes D, and the Parkinson Study Group. Markers of dopamine metabolism in Parkinson's disease. *Neurology* 1992; 42:2111-2117.
42. Furman JMR, Baloh RW, Barin K, Hain TC, Herdman S, Konrad HR, Parker SW, Van den Noort S, Altrocchi PH, Brin MF, Ferguson JH, Hanley DF, Jacobs LD, Lange DJ, Markham CH, Nuwer MR, Tindall RS, Okagaki JF. Assessment - Posturography - Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. *Neurology* 1993;43: 1261-1264.
43. Blitzer A, Brin MF, Keen MS, Aviv JE. Botulinum toxin for the treatment of hyperfunctional lines of the face. *Arch Otolaryngol Head Neck Surg* 1993;119:1018-1022.

44. † Hurowitz GI, Silver JM, Brin MF, Williams DT, Rowland LP, Johnson WG. Neuropsychiatric aspects of adult onset Tay-Sachs disease: two case reports with several new findings. *J Neuropsychiatry Clin Neurosci* 1993;5: 30-36.
45. † Borg-Stein J, Pine ZM, Miller JR, Brin MF. Botulinum toxin for the treatment of spasticity in multiple sclerosis. *Am J Phys Med Rehabil* 1993;72:364-368.
46. Parkinson Study Group. Effects of tocopherol and deprenyl on the progression of disability in early Parkinson's disease. *New England Journal of Medicine* 1993; 328:176-183.
47. Parkinson Study Group. A controlled clinical trial of lazabemide (Ro 19-6327) in untreated Parkinson's disease. *Ann Neurol* 1993; 33:350-356.
48. Adler CH, Wrabetz L, Brin MF, Hurtig HI. Cerebellar ataxia, dystonia, and tremor within a family: variable phenotypes of a single genetic disorder? *Movement Disorders* 1994;9:155-160.
49. Bressman SB, Heiman GA, Nygaard TG, Ozelius LJ, Hunt A, Brin MF, Gordon MF, Moskowitz CB, de Leon D, Burke RE, Fahn S, Risch NJ, Breakefield XO, Kramer PL. A study of idiopathic torsion dystonia in a non-Jewish family: evidence for genetic heterogeneity. *Neurology* 1994;44:283-287.
50. Bressman SB, Hunt AL, Heiman GA, Brin MF, Burke RE, Fahn S, Trugman JM, de Leon D, Kramer PL, Wilhelmsen KC, Nygaard T. Exclusion of the DYT1 locus in a non-Jewish family with early-onset dystonia. *Mov Disord* 1994;9:626-32
51. *Grillone GA, Blitzer A, Brin MF, Annino DJ, Saint Hilaire MH. Treatment of adductor laryngeal breathing dystonia with botulinum toxin. *Laryngoscope* 1994;104:30-32.
52. *,† Keen M, Blitzer A, Aviv J, Binder W, Prystowsky J, Smith H, Brin MF. Botulinum Toxin for hyperkinetic facial lines: results of a double blind placebo controlled study. *Plast Reconstr Surg* 1994;94:94-99.
53. *,† Brin MF, Stewart C, Blitzer A, Diamond B. Laryngeal botulinum toxin (BTX) injections for disabling stuttering in adults. *Neurology*, 1994;44:2262-2266.
54. *,† Brin MF, Anderson RL, Blitzer AB, Carruthers A, Cornella C, Consky E, Dubinsky R, Fahn S, Brueh BR, Hallett M, Jankovic J, Koman A, Kraft SP, Lang A, Ludlow C, Namerow NS, Rhew K, Simpson LL, Tsui J, Waters C, Woodson G. Training guidelines for the use of botulinum toxin for the treatment of neurologic disorders: Report of the Therapeutics and Technology Assessment

Subcommittee of the American Academy of Neurology. *Neurology* 1994;44:2401-2403.

55. *The Parkinson Study Group. A controlled trial of lazabemide (RO 19-6327) in levodopa treated Parkinson's disease. *Arch Neurol* 1994; 51:342-347.
56. *Kiebertz K, McDermott M, Como P, Growdon J, Brady J, Carter J, Huber S, Kanigan B, Landow E, Rudolph A, Saint-Cyr J, Stern Y, Tennis M, Thalen J, Shoulson I and the Parkinson Study Group. The effect of deprenyl and tocopherol on cognitive performance in early untreated Parkinson's disease. *Neurology* 1994; 44:1756-1759.
57. *,† Braun N, Abd A, Baer J, Blitzer A, Stewart C, Brin M. Dyspnea in dystonia. A functional evaluation. *Chest* 1995;107:1309-16.
58. *,† Mezaki T, Kaji R, Kohara N, Fujii H, Katayama M, Shimizu T, Kimura J, Brin MF. Comparison of therapeutic efficacies of type A and F botulinum toxins for blepharospasm: a double-blind, controlled study. *Neurology* 1995;45:506-8.
59. *,† Stewart C, Winfield L, Hunt A, Bressman SB, Fahn S, Blitzer A, Brin MF. Speech dysfunction in early Parkinson's disease. *Mov Disord* 1995;10:562-565.
60. *Blitzer A, Komisar A, Baredes S, Brin MF, Stewart C. Voice failure after tracheoesophageal puncture: Management with botulinum toxin. *Otolaryngol Head Neck Surg* 1995;113:668-670.
61. *Parkinson Study Group. Cerebrospinal fluid homovanillic acid in the DATATOP study on Parkinson's disease. *Arch Neurol* 1995; 52:237-245.
62. *Adler CH, Zimmerman RS, Lyons MK, Simeone F, Brin MF. Perioperative use of botulinum toxin for movement disorder-induced cervical spine disease. *Mov Disord* 1996;11:79-81.
63. *Altrocchi PH, Brin M, Ferguson JH, Goldstein, M.L.; Gorelick, P.B.; Hanley, D.F.; Lange, D.J.; Nuwer, M.R.; Van den Noort, S. Assessment of brain SPECT - Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. *Neurology* 1996;46:278-285.
64. *Ford B, Greene P, Louis ED, Petzinger G, Bressman SB, Goodman R, Brin MF, Sadiq S, Fahn S. Use of intrathecal baclofen in the treatment of patients with dystonia. *Arch Neurol* 1996; 53:1241-1246.
65. *Kurlan R, Brin MF, Fahn S. Movement disorder in reflex sympathetic dystrophy: A case proven to be psychogenic by surveillance video monitoring. *Mov Disord* 1997;12:243-245.
66. *,† Stewart CF, Allen EL, Tureen P, Diamond BE, Blitzer A, Brin MF. Adductor

- spasmodic dysphonia: standard evaluation of symptoms and severity. *J Voice* 1997;11:95-103.
67. Blitzer A, Brin MF. Use of botulinum toxin for diagnosis and management of cricopharyngeal achalasia. *Oto-Head Neck Surg* 1997;116:328-330.
 68. *,† Blitzer A, Binder WJ, Aviv JE, Keen MS, Brin MF. The management of hyperfunctional lines with botulinum toxin: A collaborative study of 210 injection sites in 162 patients. *Arch Otolaryngol* 1997;123:389-392.
 69. *Bressman SB, deLeon D, Raymond D, Greene PE, Brin MF, Fahn S, Ozelius LJ, Breakefield XO, Kramer PL, and Risch NJ. Secondary dystonia and the DYT1 gene. *Neurology* 1997;48(6):1571-7.
 70. *Lew, M.F.; Adornato, B.T.; Duane, D.D.; Dykstra, D.D.; Factor, S.A.; Massey, J.M.; Brin, M.F.; Jankovic, J.; Rodnitzky, R.L.; Singer, C.; Swenson, M.R.; Tarsy, D.; Murray, J.J.; Koller, M.; Wallace, J.D. Botulinum toxin type B (BotB): A double-blind, placebo-controlled, safety and efficacy study in cervical dystonia. *Neurology* 1997;49:701-707.
 71. *Ozelius, L.J.; Hewett, J.; Kramer, P.; Bressman, S.B.; Shalish, C.; deLeon, D.; Rutter, M.; Risch, N.; Brin, M.F.; Markova, E.D.; Limborska, S.A.; Ivanova-Smolenskaya, I.A.; McCormick, M.K.; Fahn, S.; Buckler, A.J.; Gusella, J.F.; Breakefield, X.O. Fine localization of the torsion dystonia gene (DYT1) on human chromosome 9q34: YAC map and linkage disequilibrium. *Genome Res* 1997;7:483-94.
 72. *Ozelius LJ, Hewett JW, Page CE, Bressman SB, Kramer PL, Shalish C, de Leon D, Brin MF, Raymond D, Corey DP, Fahn S, Risch NJ, Buckler AJ, Gusella JF, Breakefield XO. The early onset torsion dystonia gene (DYT1) encodes an ATP-binding protein. *Nat.Gen.* 1997;17:40-8.
 73. *Rubio, J.P.; Danek, A.; Stone, C.; Chalmers, R.; Wood, N.; Verellen, C.; Ferrer, X.; Malandrini, A.; Fabrizi, G.M.; Manfredi, M.; Vance, J.; Pericak-Vance, M.; Brown, R.; Rudolf, G.; Picard, F.; Alonso, E.; Brin, M.; Nemeth, A.H.; Farrall, M.; Monaco, A.P. Chorea-acanthocytosis: genetic linkage to chromosome 9q21. *Am.J.Hum.Genet.* 1997;61:899-908.
 74. *Almasy, L.; Bressman, S.B.; Kramer, P.L.; Greene, P.E.; Heiman, G.A.; Ford, B.; Yount, J.; Raymond, D.; de Leon, D.; Chouinard, S.; Saunders-Pullman, R.; Brin, M.F.; Kapoor, R.P.; Jones, A.C.; Shen, H.; Fahn, S.; Risch, N.J.; Nygaard, T.G. Idiopathic torsion dystonia linked to chromosome 8 in two Mennonite families. *Ann.Neurol.* 1997;42:670-673.
 75. *Kiebertz, K.; Shoulson, I.; McDermott, M.; Fahn, S.; Lang, A.; Olanow, W.; Penney, J.; Wooten, G. F.; Kurlan, R.; Gardiner, I.; Petzinger, G.; Brin, M.,

- Dillon, S., Shannon, K., Jaglin, J. A., Trosch, R., Mistura, K., Harrison, M., RostRuffner, E., Tanner, C., Singer, C., Weiner, W., Sheldon, C., Grimes, J. D., Gray, P., Hurtig, H., Hauser, R., Gauger, L., Rajput, A., Rudnitzky, R., Dobson, J., Panisset, M., Gauthier, S., Amyot, D., Perlmutter, J., Hubble, J., Barter, R., Suchowersky, O., Lew, M., Welsh, M., Marek, K., Fussell, B., Sethi, K., Ligon, K., Rao, J., Rudolph, A., Casaceli, C., Day, D., Johnston, K., and et al. Safety and efficacy of pramipexole in early Parkinson disease: A randomized dose-ranging study. *Journal of American Medical Association* 278(2), 125-130. 1997.
76. *Binder WJ, Blitzer A, Brin MF. Treatment of hyperfunctional lines of the face with botulinum toxin A. *Dermatol.Surg.* 1998;24:1198-1205.
77. *Blitzer A, Brin MF, Stewart CF. Botulinum toxin management of spasmodic dysphonia (laryngeal dystonia): a 12-year experience in more than 900 patients. *Laryngoscope* 1998;108:1435-1441.
78. *Klein C, Brin MF, de Leon D, Limborska SA, Ivanova-Smolenskaya IA, Bressman SB, Friedman A, Markova ED, Risch NJ, Breakefield XO, Ozelius LJ. De novo mutations (GAG deletion) in the DYT1 gene in two non-Jewish patients with early-onset dystonia. *Hum.Mol.Genet.* 1998;7:1133-1136.
79. *Klein C, Page CE, LeWitt P, Gordon MF, de Leon D, Awaad Y, Breakefield XO, Brin MF, Ozelius LJ. Genetic analysis of three patients with an 18p-syndrome and dystonia. *Neurology* 1999;52:649-651.
80. *Klein C, Brin MF, Kramer P, Sena-Esteves M, de Leon D, Doheny D, Bressman S, Fahn S, Breakefield XO, Ozelius LJ. Association of a missense change in the D2 dopamine receptor with myoclonus dystonia. *Proc.Natl.Acad.Sci.U.S.A.* 1999;96:5173-5176.
81. *Lazzarini A, Walters AS, Hickey K, Coccagna G, Lugaresi E, Ehrenberg BL, Picchietti DL, Brin MF, Stenroos ES, Verrico T, Johnson WG. Studies of penetrance and anticipation in five autosomal-dominant restless legs syndrome pedigrees. *Mov.Disord.* 1999;14:111-116.
82. *,†Walker RH, Spiera H, Brin MF, Olanow CW. Parkinsonism associated with Sjogren's syndrome: three new cases and a review of the literature. *Mov.Disord.* 1999;14:262-268.
83. *Klein C, Friedman J, Bressman S, Vieregge P, Brin MF, Pramstaller PP, de Leon D, Hagenah J, Sieberer M, Fleet C, Kiely R, Xin W, Breakefield XO, Ozelius LJ, Sims KB. Genetic testing for early-onset torsion dystonia (DYT1): Introduction of a simple screening method, experiences from testing of a large patient cohort, and ethical aspects. *Genet.Test.* 1999;3:323-328.
84. *Mezaki T, Kaji R, Brin MF, Hirota-Katayama M, Kubori T, Shimizu T, Kimura

J. Combined use of type A and F botulinum toxins for blepharospasm: a double-blind controlled. *Mov Disord.* 1999;14:1017-1020.

85. *,†Brin MF, Lew MF, Adler CH, Comella CL, Factor SA, Jankovic J, O'Brien C, Murray JJ, Wallace JD, Willmer-Hulme A, Koller M. Safety and efficacy of NeuroBloc (botulinum toxin type B) in type A- resistant cervical dystonia. *Neurology* 1999;53:1431-1438.
86. *Brashear A, Lew MF, Dykstra DD, Comella CL, Factor SA, Rodnitzky RL, Trosch R, Singer C, Brin MF, Murray JJ, Wallace JD, Willmer-Hulme A, Koller M. Safety and efficacy of NeuroBloc (botulinum toxin type B) in type A-responsive cervical dystonia. *Neurology* 1999;53:1439-1446.
87. *Ozelius LJ, Page CE, Klein C, Hewett JW, Mineta M, Leung J, Shalish C, Bressman SB, de Leon D, Brin MF, Fahn S, Corey DP, Breakefield XO. The TOR1A (DYT1) gene family and its role in early onset torsion dystonia. *Genomics* 1999; 62:377-384.
88. *,†Shashidharan P., Kramer B.C., Walker R.H., Olanow CW, Brin MF. Immunohistochemical localization and distribution of torsinA in normal human and rat brain. *Brain Res.* 2000;853:197-206.
89. *,† Morrison CE, Borod JC, Brin MF, Raskin SA, Germano IM, Weisz DJ, Olanow CW. A program for neuropsychological investigation of deep brain stimulation (PNIDBS) in movement disorder patients: development, feasibility, and preliminary data *Neuropsychiatry Neuropsychol.Behav.Neurol.* 2000;13:204-219.
90. * Klein C, Gurvich N, Sena-Esteves M, Fink S, Bressman S, Brin MF, Ebersole BJ, Forsgren L, Friedman J, Grimes D, Holmgren G, Kyllerman M, Lang AE, de Leon D, Leung J, Prioleau C, Raymond D, Sanner G, Saunders-Pullman R, Vieregge P, Wahlstrom J, Breakefield XO, Kramer PL, Ozelius L, Sealfon SC. Evaluation of the role of the D2 dopamine receptor in myoclonus dystonia. *Ann Neurol* 2000 (in press).
91. * Bressman SB, Sabatti C, Raymond D, de Leon D, Klein C, Kramer PL, Brin MF, Fahn S, Breakefield X, Ozelius LJ, Risch NJ. The DYT1 phenotype and guidelines for diagnostic testing [see comments]. *Neurology* 2000;54:1746-1752.
92. * Shashidharan P, Good PF, Hsu A, Perl D, Brin MF, Olanow CW. TorsinA accumulation in Lewy Bodies in sporadic Parkinson's disease. *Brain Res.* 2000;877:379-381.

B. Books, reviews, chapters, letters and editorials:

1. † Brin MF, Traber MG. Vitamin E deficiency and neurological disease. *Laboratory Management* 1985;23:57-67.

2. † Brin MF, Fahn S, Moskowitz CB, Friedman A, Shale HM, Green PE, Blitzer A, List T, Lange D, Lovelace RE, McMahon D. Localized injections of botulinum toxin for the treatment of focal dystonia and hemifacial spasm. *Adv Neurol* 1988;599-608.
3. † Brin MF, Moskowitz CB, Fahn S. The Dystonia Clinical Research Center Tissue Resource Facility. *Adv Neurol* 1988;50:215-222.
4. Lange DJ, Brin M, Fahn S, Lovelace RE. Distant effects of locally injected botulinum toxin: incidence and course. *Adv Neurol* 1988;50:609-614.
5. Bressman SB, de Leon D, Brin MF, Risch N, Fahn S. The pattern of inheritance of dystonia among Ashkenazi Jews. *Adv Neurol* 1988;50:45-56.
6. Kramer PL, Ozelius LO, Brin MF, Bressman SB, Moskowitz CB, Fahn S, Kidd KK, Guesella J, Breakefield XO. Molecular genetics of an autosomal dominant form of Torsion Dystonia. *Adv Neurol* 1988;50:57-66.
7. † Brin MF, de Yebenes J, Fahn S. Neuroacanthocytosis (Levine syndrome). *Current Opinion in Neurol and Neurosurg* 1988;1:332-334.
8. † Brin MF, Younger D. Neurologic disorders and aspiration. *Oto Clinics of North Amer* 1988;691-699.
9. Blitzer A, Brin MF. Spastic dysphonia (laryngeal dystonia). Gates G (ed). *Current therapy in otolaryngology - head and neck surgery*. 1989;4.
10. Blitzer A, Brin MF, Fahn S. Botulinum toxin injections for lingual dystonia. *Laryngoscope* 1991;101: 799.
11. † Brin MF. Interventional neurology: treatment of neurological conditions with local injections of botulinum toxin. *Arch de Neurobiol (Spain)* 1991;54 (Suppl 3):7-23.
12. † Brin MF, Fahn S, Blitzer A, Ramig LO, Stewart C. Movement Disorders of the Larynx. In Blitzer A, Brin MF, Sasaki CT, Fahn S, Harris KS (eds): Neurological disorders of the larynx. Thieme:New York, 1992: 248-276.
13. † Brin MF, Blitzer A, Stewart C, Fahn S. Treatment of spasmodic dysphonia (laryngeal dystonia) with local injections of botulinum toxin: review and technical aspects. In Blitzer A, Brin MF, Sasaki CT, Fahn S, Harris KS (eds): Neurological disorders of the larynx. Thieme:New York, 1992:214-228.
14. † Brin MF. Advances in dystonia: genetics and treatment with botulinum toxin. In Smith B, Adelman G. *Neuroscience Year, Supplement to the Encyclopedia of*

Neuroscience. Birkhauser: Boston. 1992, 56-58.

15. Lang A, Quinn N, Marsden CD, Findley L, Koller W, Brin M, Fahn S. Essential tremor [letter; comment]. *Neurology* 1992;42: 1432-1434.
16. Blitzer A, Brin MF. Neurolaryngology. In: Cummings CW, Fredrickson JM, Harker LA, Krause CJ, Schuller DE (eds) *Otolaryngology - Head and Neck Surgery*. Mosby Year Book, S. Louis, 1992; 2053-2060.
17. Fahn S, Breakefield XO, and the Dystonia Genetics Research Group. Idiopathic torsion dystonia in Ashkenazi Jews: autosomal dominant inheritance pattern of a gene located on chromosome 9q32-34. In Bonne-Tamir B (ed): *New Perspectives on Genetic Markers and Disease Among Jewish People*. London: Oxford University Press, 1992.
18. † Brin MF, Blitzer A, Stewart C, Pine Z, Borg-Stein J, Miller J, Viswanath NS, Rosenfield DB. Disorders with excessive muscle contraction: Candidates for treatment with intramuscular botulinum toxin ("botox"). In: DasGupta BR (ed). *Botulinum and Tetanus Neurotoxins: Neurotransmission and Biomedical Aspects*. Plenum: New York, 1993: 559-576.
19. † Brin MF. Acanthocytosis. In: Goetz CG, Tanner CM, Aminoff MJ (eds): *Handbook of Clinical Neurology*. North-Holland:Amsterdam, 1993:271-299.
20. † Brin MF. Current concepts in the management of torticollis (cervical dystonia). In Johnson RT, Griffin JW, eds. *Current Therapy in Neurological Diseases*, 4th ed. Mosby - YearBook, Philadelphia, 1993.
21. † Brin MF, Blitzer A. Botulinum toxin - dangerous terminology errors (letter). *J Royal Soc Med* 1993;86:494.
22. Lange DJ, Brin MF, Greene P, Lovelace RE, Fahn S. Distant Effects of Locally Injected Botulinum Toxin - A Double-Blind Study of Single Fiber EMG Changes - A Reply. *Muscle Nerve* 1993;16: 677.
23. Blitzer A, Brin MF. Botulinum Toxin in the Management of Adductor and Abductor Spasmodic Dysphonia. In: Friedman M, Tucker HM (eds) *Operative Techniques in Otolaryngology-Head and Neck Surgery*. W.B. Saunders, Philadelphia, pp 199-206, 1993.
24. Blitzer A, Brin MF. Evaluation and management of hyperfunctional muscular disorders of the head and neck. *Adv Oto-Head Neck Surg* 1993;7:1-28.
25. *,† Brin MF, Blitzer A, Herman S, Stewart C. Oromandibular dystonia: treatment of 96 patients with botulinum toxin A. In: Jankovic J, Hallett M, eds. *Botulinum toxin treatment*. Marcel Dekker, New York, 1994, pp 429-436.

26. Blitzer A, Brin MF. The evaluation and management of abductor laryngeal dysphonia. In: Jankovic J, Hallett M, eds. Botulinum toxin treatment. Marcel Dekker, New York, 1994, pp 451-460.
27. Greene PE, Brin MF, Fahn SF, Blitzer A. Botulinum toxin in dystonia. In: Marsden CD, Fahn S. Movement Disorders 3. London: Butterworth, 1994, pp 477-502.
28. *,† Brin MF, Jankovic J, Comella C, Blitzer A, Tsui J, Pullman SL. Treatment of dystonia using botulinum toxin. In: Kurlan, ed. Treatment of Movement Disorders. Lippincott: Phila 1995:183-247.
29. *,† Brin MF, Blitzer A, Herman S, Stewart C. Oro-facio-mandibular and lingual dystonia (Meige syndrome): botulinum toxin treatment. In: Moore AP, ed. Handbook of botulinum toxin treatment. Blackwell Scientific, Oxford, 1995, (in press).
30. *,† Brin MF, Blitzer A, Stewart C. Vocal Tremor. In: Findley LJ, Koller WC (eds) Handbook of Tremor Disorders. Dekker, New York 1995:495-520.
31. *,† Stewart CS, Brin MF, Blitzer A. Spasmodic Dysphonia. In: Ferrand CT, Bloom RL (eds), Introduction to Organic and Neurogenic Disorders of Communication: Current Scope of Practice. Needham Heights: Allyn & Bacon, 1997:301-318.
32. *,† Brin MF, Vapnek JM. Treatment of vaginismus with botulinum toxin injections. Lancet. 1997;349(9047):252-3.
33. *,† Brin MF. Botulinum toxin: new and expanded indications. Eur.J.Neurol. 1997;4 (suppl 2):59-66.
34. *,† Brin M. F. (Editor). Spasticity: Etiology, Evaluation, Management, and the Role of Botulinum Toxin Type A: A training syllabus developed by the Spasticity Study Group. Muscle Nerve 1997;20 (suppl 6): S1-S231.
35. *,† Brin M. F. Botulinum toxin: chemistry, pharmacology, toxicity, and immunology. Muscle Nerve 1997;20 (suppl 6): S146-68.
36. *,† Brin M. F. and The Spasticity Study Group. Dosing, administration, and a treatment algorithm for use of botulinum toxin A for adult-onset spasticity. Muscle Nerve 1997;20 (suppl 6): S208-20.
37. * Jankovic J. and M. F. Brin. Botulinum toxin: historical perspective and potential new indications. Muscle Nerve 1997;20 (suppl 6): S129-45.

38. *,† Brin MF. Treatment of dystonia. In: Jankovic J, Tolosa E (eds). *Parkinson's Disease and Movement Disorders*. New York: Williams & Wilkins; 1998, 553-578.
39. *,† Brin MF. Pharmacological treatment of movement disorders. In: Germano I, ed. *Neurosurgical Treatment of Movement Disorders*. Lebanon: Amer.Assoc.Neurol.Surgeons, 1998:83-104.
40. *,† Brin MF, Blitzer A, Stewart C. Laryngeal dystonia (spasmodic dysphonia): Observations of 901 patients and treatment with botulinum toxin. *Adv.Neurol.* 1998;78:237-252.
41. *,† Brin M. F. and W. C. Koller. Epidemiology and genetics of essential tremor. *Movement Disorders*, 1998;13 (Suppl 3), 55-63.
42. *Deuschl G, Bain P, Brin M. Consensus statement of the Movement Disorder Society on Tremor. Ad Hoc Scientific Committee. *Mov.Disord.* 1998;13 Suppl 3:2-23.
43. *Jenner PG, Brin MF. Levodopa neurotoxicity: experimental studies versus clinical relevance. *Neurology* 1998;50:S39-S43
44. *Ozelius LJ, Hewett JW, Page CE, Bressman SB, Kramer PL, Shalish C, de Leon D, Brin MF, Raymond D, Jacoby D, Penney J, Risch NJ, Fahn S, Gusella JF, Breakefield XO. The gene (DYT1) for early-onset torsion dystonia encodes a novel protein related to the Clp protease/heat shock family. *Adv.Neurol.* 1998;78:93-105.
45. *Ford B, Greene PE, Louis ED, Bressman SB, Goodman RR, Brin MF, Sadiq S, Fahn S. Intrathecal baclofen in the treatment of dystonia. *Adv.Neurol.* 1998;78:199-210.
46. *Bressman SB, de Leon D, Raymond D, Greene PE, Brin MF, Fahn S, Ozelius LJ, Breakefield XO, Kramer PL, Risch NJ. The role of the DYT1 gene in secondary dystonia. *Adv.Neurol.* 1998;78:107-115.
47. *Blitzer A, Binder WJ, Brin MF. Management of Facial Wrinkles with Botulinum Toxin Injections. In: Krespi YP, ed. *Office-Based Surgery of the Head and Neck*. New York: Lippincott-Raven, 1998:251-254.
48. *,† Brin MF. Advances in Dystonia: Classification, Genetics and Therapeutics, *Neuroscience Year. Supplement to the Encyclopedia of Neuroscience*, 1999.
49. *,† Brin MF. Botulinum toxin for motor disorders. In: Younger DS, ed. *Textbook of Motor Disorders*. Philadelphia: Lippincott Williams & Wilkins, 1999:515-522.

50. *Stewart CF, Blitzer A, Brin MF. Evaluation and management of swallowing and voice disorders. In: Younger DS, ed. Textbook of Motor Disorders. Philadelphia: Lippincott Williams & Wilkins, 1999:477-492.
51. *,† Brin MF, Benabou R. Cervical dystonia (torticollis). Current Treatment Options in Neurology 1999;1:33-43.
52. *Blitzer A, Binder WJ, Brin MF. Botulinum toxin injections for facial lines and wrinkles: Technique. In: Blitzer A, Binder WJ, Boyd BJ, Carruthers A, eds. Management of Facial Lines and Wrinkles. New York: Lippincott Williams & Wilkins, 2000:303-313.
53. *,† Brin MF. Botulinum toxin therapy: Basic science and overview of other therapeutic applications. In: Blitzer A, Binder WJ, Boyd JB, Carruthers A, eds. Management of Facial Lines and Wrinkles. New York: Lippincott Williams & Wilkins, 2000:279-302.
54. *Olanow C. W. and M. F. Brin. The role of deep brain stimulation as a surgical treatment for Parkinson's disease. Neurology, 2000 (in press).
55. *,† Brin MF. Physician and Patients in managing Parkinson's disease. In: Cote L, Sprinzeles LL, Elliott R, Kutscher AH, eds. Parkinson's Disease and Quality of Life. Binghamton: Haworth Press, 2000:11-13.
56. *Bain P, Brin M, Deuschl G, Elble R, Jankovic J, Findley L, Koller WC, Pahwa R. Criteria for the diagnosis of essential tremor. Neurology 2000;54:S7
57. *Koller WC, Hristova A, Brin M. Pharmacologic treatment of essential tremor. Neurology 2000;54:S30-S38
58. *Comella, C.L., Brin, M.F., Brownlee, H.J. Diagnosis and Treatment of Parkinson's Disease: A Handbook for Primary Care Physicians. Chicago: Rush Presbyterian Medical Center, 2000

*: Publication subsequent to promotion to Associate Professor
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